Randy S. Bethiel et al.

Application No.: 10/700,936

AMENDMENTS TO THE CLAIMS

Please replace all prior versions and listings of claims with the amended claims as follows:

I. (Previously presented) A compound of formula I:

or a pharmaceutically acceptable salt thereof, wherein:

 W^1 is nitrogen or CH, W^2 is nitrogen or C-(U)₀R^U, and W^3 is nitrogen or C-(V)₄R^Y; p and q are each independently 0 or 1;

 R^{U} and R^{V} are each independently R or Ar^{1} ;

U and V are each independently a bond or a C_{1.6} alkylidene chain, wherein up to two methylene units of the chain are optionally and independently replaced by CO, CO₂, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, NRCO₂, NRCONR, SO, SO₂, NRSO₂, SO₂NR, NRSO₂NR, O, S, or NR:

each occurrence of R is independently hydrogen or an optionally substituted C₁-C₄ aliphatic, or two R bound to the same nitrogen atom are optionally taken together with the nitrogen atom to form a 3-7 membered saturated, partially unsaturated, or fully unsaturated ring having 0-2 additional heteroatoms independently selected from nitrogen, oxygen, or sulfur;

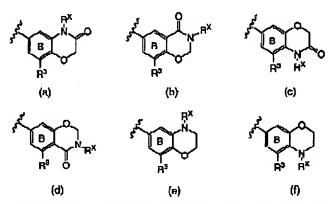
Art is a 5-7 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or

Randy S. Bethiel et al.

Application No.: 10/700,936

sulfur; wherein Ar¹ is optionally substituted with m independent occurrences of Z-R⁵; wherein m is 0-5, Z is a bond or is a C₁-C₄ alkylidene chain wherein up to two methylene units of Z are optionally replaced by CO, CO₂, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, NRCO₂, NRCONR, SO, SO₂, NRSO₂, SO₂NR, NRSO₇NR, O, S, or NR; and each occurrence of R⁵ is independently bydrogen, an optionally substituted aliphatic, heteroaliphatic, aryl or heteroaryl group, halogen, NO₂, CN, OR, SR, N(R)₂, NRCOR, NRCON(R)₂, NRCO₂R, COR, CO₂R, OCOR, CON(R)₂, OCON(R)₂, SOR, SO₂R, SO₂N(R)₂, NRSO₂R, NRSO₂N(R)₂, COCOR, or COCH₂COR;

R¹ and R² are taken together and fused to ring B to form a heterocyclic moiety selected from one of formulae (a) through (f):



wherein each occurrence of R^X is independently hydrogen, QR, or Q_nAr¹; n is zero or one; and Q is an optionally substituted C₁₋₄ alkylidene chain wherein one methylene unit of Q is optionally replaced by CO, CO₂, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, NRCO₂, NRCO₂, NRCO₃, NRCO₃, NRSO₂, NRSO₂, NRSO₂, NRSO₂NR, O, S, or NR;

 R^3 is hydrogen, halogen, QR, Q_nCN, Q_nNO₂, or Q_nAr¹; and R^4 is Ar¹, or T-Ar¹;

Randy S. Bethiel et al.

Application No.:

10/700,936

wherein T is a C₁₋₂ alkylidene chain wherein one methylene unit of T is optionally replaced by CO, CO₂, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, NRCO₂, NRCONR, SO, SO₂, NRSO₂, SO₂NR, NRSO₂NR, O, S, or NR.

- 2. (Previously presented) The compound of claim 1, wherein R^1 and R^2 taken together form the heterocyclic moiety of formula (a) and R^2 is hydrogen or optionally substituted $C_{1.6}$ aliphatic.
- 3. (Original) The compound of claim 1, wherein R^X is hydrogen, methyl, ethyl, propyl, n-butyl, tert-butyl, pentyl, cyclopentyl, hexyl, cyclohexyl, C_{1-6} alkyl substituted with $N(R)_2$, or C_{1-6} alkyl substituted with Ar^1 .
- 4. (Original) The compound of claim 1, wherein R^X is hydrogen, methyl, or C_{1.2}alkyl substituted with a group selected from optionally substituted phenyl, pyridyl, morpholino, piperidinyl, or piperazinyl.
- 5. (Original) The compound of claim 1, wherein R³ is hydrogen, halogen, QR or QAr¹, wherein Q is a C₁₋₃ alkylidene chain wherein one methylene unit of Q is optionally replaced by -O-, -S-, -NHCO-, or -NR-, and Ar¹ is an optionally substituted 5-6 membered saturated, partially unsaturated, or fully unsaturated ring having 0-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur.
- (Original) The compound of claim 1, wherein R³ is hydrogen, OH, OCH₃,
 OCH₂CH₃, NHCOMe, NH₂, NH(C_{1.4} aliphatic), N(C_{1.4} aliphatic)₂, O(CH₂)₂morpholin-4-yl,
 O(CH₂)₂NH₂, O(CH₂)₂NH(C_{1.4} aliphatic), O(CH₂)₂N(C_{1.4} aliphatic)₂, Rr. Cl. cr F.
- 7. (Original) The compound of claim 1, wherein R³ is hydrogen.

Randy S. Berhiel et al.

Application No.:

10/700,936

- 8. (Original) The compound of claim 1, wherein R⁴ is a 6-membered saturated, partially unsaturated, or aryl ring having 0-3 nitrogens, a 9-10 membered bicyclic aryl ring having 0-2 nitrogen atoms, or a 5 membered heteroaryl ring having 2-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein each ring is optionally substituted.
- 9. (Original) The compound of claim 1, wherein R⁴ is optionally substituted phenyl, cyclohexyl, naphthyl, pyridyl, pyrimidinyl, triazinyl, thiazolyl, thiadiazolyl, pyrazolyl, isoxazolyl, indazolyl, or benzimidazolyl.
- (Original) The compound of claim 1, wherein R⁴ is an optionally substituted phenyl group.
- 11. (Original) The compound of claim 8, wherein each occurrence of Z is independently a bond or a C₁₋₄ alkylidene chain wherein one methylene unit of Z is optionally replaced by O-, -S-, -SO₂-, or -NH-; and each occurrence of R⁵ is independently hydrogen, C₁₋₆ aliphatic, halogen, NO₂, OR, N(R)₂, or optionally substituted phenyl, pyridyl, or pyrimidinyl.
- 12. (Previously presented) The compound of claim 8, wherein each occurrence of ZR⁵ is independently Cl, F, Br, methyl, ethyl, t-butyl, isopropyl, cyclopropyl, nitro, CN, OMe, OEt, CF₃. NH₂, phenyl, benzyl, benzyloxy, OH, methylenedioxy, SO₂NH₂, CONH₂, CO₂Me, phenoxy, O-pyridinyl, SO₂phenyl, nitrophenoxy, aminophenoxy, S-dimethylpyrimidine, NHphenyl, NH-methoxyphenyl, pyridinyl, phenol, chloro-fluoro-phenyl, dimethylaminophenyl, CF₃-phenyl, dimethylphenyl, chlorophenyl, fluorophenyl, methoxyphenoxy, chlorophenoxy, ethoxyphenoxy, and fluorophenoxy.
- 13. (Original) The compound of claim 1, wherein $(U)_pR^V$ and $(V)_qR^V$ are each independently hydrogen, halogen, NO₂, CN, OR, SR or N(R)₂, or C₁₋₄aliphatic optionally substituted with oxo, OR, SR, N(R)₂, halogen, NO₂ or CN.

Randy S. Bethiel et al.

Application No.:

10/700,936

- 14. (Original) The compound of claim 1, wherein $(U)_p R^U$ and $(V)_q R^V$ are each independently hydrogen, Me, OH, or OMe.
- 15. (Original) The compound of claim 1, wherein W^1 is N or CH and compounds have the structure of Formula Ia or Ib:

or a pharmaceutically acceptable salt thereof.

16. (Previously presented) The compound of claim 15, wherein R⁴ is an optionally substituted phenyl group and compounds have the structure of Formula II2 or IIb:

or a pharmaceutically acceptable salt thereof.

17. (Previously presented) The compound of claim 16, wherein R³ is hydrogen, and compounds have the structure of Formula IIIa or IIIb:

Randy S. Bethiel et al.

Application No.: 10/700,936

or a pharmaceutically acceptable salt thereof.

18. (Previously presented) The compound of claim 16, wherein R³ is hydrogen, and R¹ and R² taken together form the heterocyclic moiety of formula (a) and compounds have the structure of Formula IVa or IVb:

or a pharmaceutically acceptable salt thereof.

- 19. (Previously presented) The compound of claim 15, wherein
- i) R^1 and R^2 taken together form the heterocyclic moiety of formula (a); where R^X is defined according to one of the following groups:
 - (a) hydrogen or optionally substituted C1.6aliphatic;
 - (b) hydrogen, methyl, ethyl, propyl, n-butyl, tert-butyl, pentyl, cyclopentyl, hexyl, cyclohexyl, C_{1-6} alkyl substituted with $N(R)_2$, or C_{1-6} alkyl substituted with Ar^1 ; or

Randy S. Bethiel et al.

Application No.:

10/700,936

(c) hydrogen, methyl, or C₁₋₇alkyl substituted with a group selected from equicanally substituted phenyl, pyridyl, morpholino, piperidinyl, or piperazinyl.

- ii) R³ is defined according to one of the following groups:
 - (a) hydrogen, halogen, QR or QAr¹, wherein Q is a C₁₋₃ alkylidene chain wherein one methylene unit of Q is optionally replaced by -O-, -S-, -NHCO-, or -NR-, and Ar¹ is an optionally substituted 5-6 membered saturated, partially unsaturated, or fully unsaturated ring having 0-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur;
 - (b) hydrogen, OH, OCH₃, OCH₂CH₃, NHCOMe, NH₂, NH(C₁₋₄ aliphatic), N(C₁₋₄ aliphatic)₂, O(CH₂)₂morpholin-4-yl, O(CH₂)₂NH₂, O(CH₂)₂NH(C₁₋₄ aliphatic), O(CH₂)₂N(C₁₋₄ aliphatic)₂, bromo, chloro, or fluoro; or (c) hydrogen;
- iii) R4 is defined according to one of the following groups:
 - (a) a 6-membered saturated, partially unsaturated, or aryl ring having 0-3 nitrogens, a 9-10 membered bicyclic aryl ring having 0-2 nitrogens, or a 5 membered heteroaryl ring having 2-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is optionally substituted with (ZR⁵)_m;
 - (b) an optionally substituted ring selected from phenyl, cyclohexyl, naphthyl, pyridyl, pyrimidinyl, triazinyl, thiazolyl, thiadiazolyl, pyrazolyl, isoxazolyl, indazolyl, or benzimidazolyl, wherein said ring is optionally substituted with (ZR⁵)_m; or
 - (c) an optionally substituted phenyl group, wherein said phenyl group is optionally substituted with $(ZR^5)_m$;
- iv) W^1 , W^2 and W^3 are defined according to one of the following groups:
 - (a) W¹ is nitrogen or CH, W² is nitrogen or C-(U)_pR^U, and W³ is nitrogen or C-(V)_qR^V;

Randy S. Bethiel et al.

Application No.:

10/700.936

- (b) W1 is mirrogen or CH, W2 is C-(U), R1, and W3 is C-(V), R'; or
- (c) W1 is nitrogen or CH and W2 and W3 are each CH; and
- v) $(U)_p R^U$ and $(V)_q R^V$ groups are defined according to one of the following groups:
 - (a) hydrogen, halogen, NO₂, CN, OR, SR or N(R)₂, or C_{1.4}aliphatic optionally substituted with oxo, OR, SR, N(R)₂, halogen, NO₂ or CN;
 - (b) hydrogen, Mc, OH, OMe or N(R)2; or
 - (c) both (U)₀R^U and (V)₀R^V are hydrogen.
- 20. (Previously presented) The compound of any one of claims 16, 17, 18 or 19, wherein each occurrence of Z is independently a bond or a C₁₋₄ alkylidene chain wherein one methylene unit of Z is optionally replaced by -O-, -S-, -SO₂-, or -NH-; and each occurrence of R⁵ is independently hydrogen, C₁₋₆ aliphatic, halogen, NO₂, OR, N(R)₂, or optionally substituted phenyl, pyridyl, and pyrimidinyl.
- 21. (Previously presented) The compound of claim 20, wherein each occurrence of ZR⁵ is independently Cl, F, Br, methyl, ethyl, t-butyl, isopropyl, cyclopropyl, nim, CN, OMe, OEt, CF₃, NH₂, phenyl, benzyloxy, OH, methylenedioxy, SO₂NH₂, CONH₂, CO₂Me, phenoxy, O-pyridinyl, SO₂phenyl, nitrophenoxy, aminophenoxy, S-dimethylpyrimidine, NHphenyl, NH-methoxyphenyl, pyridinyl, phenol, chloro-fluoro-phenyl, dimethylaminophenyl, CF₃-phenyl, dimethylphenyl, chlorophenyl, fluorophenyl, methoxyphenoxy, chlorophenoxy, ethoxyphenoxy, or fluorophenoxy.
- 22. (Previously presented) The compound of claim 18 having the formula IVa, wherein R^X is hydrogen or optionally substituted C₁₋₆aliphatic; m is 0, 1 or 2; and ZR³ is Cl, F, Br, methyl, ethyl, t-butyl, isopropyl, cyclopropyl, nitro, CN, OMe, OEt, CP₃, NH₂, phenyl, benzyl, benzyloxy, OH, methylenedioxy, SO₂NH₂, CONH₂, CO₂Me, phenoxy, O-pyridinyl, SO₂phenyl, nitrophenoxy, aminophenoxy, S-dimethylpyrimidine, NHphenyl, NH-methoxyphenyl, pyridinyl, phenol, chloro-fluoro-phenyl, dimethylaminophenyl, CP₃-phenyl,

Randy S. Bethiel et al.

Application No.:

10/700,936

dimethylphenyl, chlorophenyl, fluorophenyl, methoxyphenoxy, chlorophenoxy, ethoxyphenoxy, or fluorophenoxy.

23. (Previously presented) The compound of claim 1, selected from one of the following compounds:

Randy S. Bethiel et al.

No.: 10/700,936

Randy S. Bethiel et al.

Application No.: 10/700,936

Randy S. Bethiel et al. 10/700,936

Randy S. Bethiel et al.

o.: 10/700,936

Randy S. Bethiel et al.

10/700,936

Randy S. Bethiel et al.

.: 10/700,936

Randy S. Bethiel et al.

10/700,936

Randy S. Bethiel et al.

Application No.: 10/700,936

Randy S. Bethiel et al. 10/700,936

ion No.: 10/700,930

Randy S. Bethiel et al.

tion No.: 10/700,936

Randy S. Bethiel et al. 10/700,936

Application No.:

Randy S. Bethiel et al.

10/700,936

Randy S. Bethiel et al.

Application No.: 10/700,936

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- 24. (Original) A pharmaceutical composition comprising a compound according to claim 1, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.
- 25. (Canceled)
- 26. (Currently amended) A method of inhibiting JAK-3 kinase activity in a hiological sample; [[:]]

(a) a patient; or

(b) a biological sample;

which method comprises administering to end patient, or contacting said biological sample with a compound of claim 1 or a composition comprising said compound.

- 27. (Canceled)
- 28. (Currently amended) A method of treating or lessening the severity of a The method of claim 27, wherein the disease or disorder [[is]] selected from an allergic or type I hypersensitivity reaction, asthma, transplant rejection, graft versus host disease, rheumatoid arthritis, amyotrophic lateral selectesis, multiple selectesis, Familial amyotrophic lateral selectesis (FALS), or leukemia, or lymphoma comprising administering to a subject in need thereof a compound of claim 1 or a composition comprising said compound.

Randy S. Bethiel et al.

Application No.:

10/700,936

29. The method of claim 28, comprising the further step of administering to said patient an additional therapeutic agent selected from a chemotherapeutic or anti-proliferative agent, a treatment for Alzheimer's Disease, a treatment for Parkinson's Disease, an agent for treating Multiple Selectoria (MS), a treatment for asthma, an agent for treating schizophrenia, an anti-inflammatory agent, or an immunomodulatory or immunosuppressive agent, a neurotrophic factor, an agent for treating cardiovascular disease, an agent for treating destructive bone disorders, an agent for treating liver disease, an agent for treating a blood disorder, or an agent for treating an immunodeficiency disorder, wherein

said additional therapeutic agent is appropriate for the disease being treated; and said additional therapeutic agent is administered together with said composition as a single dosage form or separately from said composition as part of a multiple dosage form.